POLICY AND COMMUNICATIONS BULLETIN
THE CLINICAL CENTER

Medical Administrative Series

M77-2 (rev.) 21 April 1997

MANUAL TRANSMITTAL SHEET

SUBJECT: Informed Consent

1. Explanation of Material Transmitted: This issuance transmits the revised policy and procedures of the Warren Grant Magnuson Clinical Center for obtaining informed consent from individuals who come to the Clinical Center to participate in research. This policy was reviewed by the Medical Executive Committee on 18 February 1997, along with MAS No. 84-2, "Inclusion in the Medical Record: Informed Consents Pertaining to Research Protocols"; the two policies were combined and approved with substantive changes (see following page for summary of changes).

2. Material Superseded: MAS No. 77-2, dated 29 July 1977
and
MAS No. 84-2, dated 3 April 1984

3. Filing Instructions: Informed Consent Section

Remove: No. 77-2, dated 29 July 1977
and
No. 84-2, dated 3 April 1984

Insert: No. M77-2 (rev.), dated 21 April 1997

DISTRIBUTION

Physicians, Dentists, and Other Practitioners Participating in Patient Care

Specific changes include:

a. Reorganization of the previous policy issuance for clarification, including:

   - a clear statement of the policy
   - explanation of to whom the policy applies
   - statement about the responsibility of investigators
   - separate sections for definitions and for procedures

b. Additional explanation of the justification for informed consent

c. Procedure section divided into: 1) the Process, and 2) the Written Document

d. Updated listing of elements to be included in written consent document

e. Clarified and updated section on Responsibility for Obtaining Informed Consent

f. New sections on: approval of informed consent; oral consent and non-English consent; and, consent for postmortem examination; consent from someone not at the CC

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Table of Contents:

Attachment A:

NIH 2514-1 - Consent to Participate in a Clinical Research Study

NIH 2514-2 - Minor Patient's Assent to Participate in a Clinical Research Study

NIH 2514-3 - Inclusion of HIV Testing in Consent to Participate in a Clinical Research Study

BACKGROUND

Ethical considerations and Federal regulations [codified in Title 45, Code of Federal Regulations, Part 46 (45 CFR 46), "Protection of Human Subjects"] require that investigators obtain the subject's informed consent before any research procedures are initiated. This requirement is articulated in the National Institutes of Health's Assurance of Compliance (Multiple Project Assurance or MPA) with DHHS Regulations for the Protection of Human Subjects (45 CFR 46), also found in M93-1 "Research Involving Human Subjects at the Clinical Center."

The ethical principle of respect for persons requires that subjects be given the opportunity to choose what shall and shall not happen to them. Informed consent requires: (1) disclosure of relevant information about the research to prospective subjects; (2) their comprehension of the information, and (3) their voluntary agreement, free of coercion and undue influence, to participate in research.

POLICY

Each person participating in research activities at the Warren Grant Magnuson Clinical Center of the National Institutes of Health (NIH) (hereafter referred to as the Clinical Center), or their legally authorized representative, will grant informed consent prior to beginning study participation by signing a “Consent to Participate in a Clinical Research Study,” (NIH-2514-1) or “Minor Patient’s Assent to Participate in a Clinical Research Study,” (NIH-2514-2). (Attachment A). This includes providing consent for screening procedures performed to determine eligibility for research participation, whether the procedures are or are not clinically indicated. The signed consent documents will be maintained in the patient’s medical record under section IV, divider “Protocol Consent,” housed in the Medical Record Department.

Investigators are responsible for informing potential research subjects of the nature of the study, the risks and benefits of participation, and all information necessary for the subjects to make a considered decision whether or not to participate. Investigators are responsible, also, for assessing that prospective and currently-enrolled subjects understand the information provided and that individuals are giving consent which is voluntary, and free of coercion or undue influence.

This policy applies to adults providing their own informed consent as well as to parents, guardians, or other legally authorized representatives of minors or of adults unable to provide their own consent.

For a minor to participate in research, permission must be obtained from parent(s) or legal guardian(s), and assent obtained from the child (when capable of giving assent as determined by the IRB). Investigators are responsible for informing parent(s) or guardian(s) about the research as well as assessing their understanding and voluntariness as described in this policy. For research involving minimal risk or involving greater than minimal risk but a prospect of direct benefit to the individual child, the permission and signature of one parent is generally sufficient, if approved by the IRB. For any other IRB approved research with children (i.e., greater than minimal risk, no prospect of direct benefit) the permission and signature of both parents is required unless one parent is deceased, unknown, legally incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child. Refer to MAS 92-5, "Research Involving Children and Children's Assent to Research," for additional requirements and procedures for research with children.

For research involving adults who are cognitively unable to provide their own consent, permission must be obtained from an individual designated by the adult subject as his or her durable power of attorney for health care (Health care "agent" according to the Health Care Decisions Act of Maryland), or by a surrogate as authorized under the laws of the state of Maryland. Investigators are responsible for informing this legally authorized representative about the research as well as assessing his or her understanding and voluntariness as described in this policy. Under current policy, three levels of research risk approved by the IRB are approved research risk are permitted for adults who cannot provide their own consent: 1) research involving minimal risk; 2) research involving greater than minimal risk but having a prospect of direct benefit to the individual subject; and 3) research involving greater than minimal risk with no prospect of direct benefit to the subject but likely to yield generalizable knowledge about the subject's disorder or condition. In addition to the requirements set forth in this policy, additional policies and procedures as contained in MAS 87-4, "Consent Process in Research Involving Impaired Human Subjects," should be followed.

DEFINITIONS

An adult is anyone 18 years of age or older. A minor who is married or a parent is also considered an adult at the Clinical Center or in the state of Maryland, for purposes of providing consent.

Informed consent is voluntary consent given by a person who has legal capacity to give consent, and who exercises free power of choice, without the intervention of any element of force, fraud, deceit, duress, constraint or coercion, and who has sufficient knowledge and understanding of the nature of the proposed research, the anticipated risks and potential benefits, and the requirements of the research as to be able to make an informed decision. (Modified from Levine, R.J., Ethics and Regulation of Clinical Research, 1986.)

An investigational procedure is any intervention performed for the purpose of research, whether conducted as part of a research protocol or screening for research eligibility, and whether or not the intervention is clinically indicated.

A non-investigational procedure is any intervention that is not being performed as part of a research study but is performed to meet the clinical needs or medical requirements of the individual who is a research subject or being screened for research participation at the CC.

Research means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. (45 CFR 46.102 (d).)

Human subject means a living individual about whom an investigator (whether professional or student) conducting research obtains:

1) data through intervention or interaction with the individual, or
2) identifiable private information. (45 CFR 46.102 (f).)

Decisionally capacitated means that the subject is an adult (as defined previously) and has sufficient mental capacity to understand the information that is provided and to make a reasoned decision whether or not to participate in the study.

Legally authorized representative means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in research.

PROCEDURES

I. The Process of Informed Consent

Informed consent by research subjects is a process that includes discussion of the research study with the Principal Investigator (PI) or others as appropriate, and signing the written informed consent document. Ongoing discussion with and education of subjects about the study should continue after the informed consent document is signed.

Informed consent begins when an individual enters into conversation with a member of the NIH Staff about participation in an NIH Intramural Research Program (IRP) protocol and continues until the individual completes study participation, withdraws consent, or is withdrawn from the study.

Information shall be offered in a manner which the subject understands. Each subject's understanding of the information should be assessed. The subject should have sufficient time, information and opportunity to consider, free of coercion or undue influence, whether or not to participate.

II. The Written Informed Consent Document

NIH Consent document Form 2514-1, "Consent to Participate in a Clinical Research Study," is used for all research conducted at the Clinical Center. Form 2514-1 is available from IRB coordinators electronically from the Clinical Center's Homepage, or the Protocol Coordination Service Center. Protocol consent documents are time limited, and must be signed by the patient within the date parameters identified on the last page of the consent.

The consent form must include all elements required by 45 CFR 46.116 and any other information needed for an individual to be fully informed about study participation. Consent documents shall be written, in non-technical language that can be understood by the layperson, and shall include the following elements:

1) A statement that the study involves research;

2) An explanation of the purpose of the research, an invitation to participate and an explanation of why the subject was selected, and the expected duration of the subject's participation;

3) A description of procedures to be followed and identification of which procedures are investigational and which might be provided as standard care to the subject in a community setting. Use of research methods such as randomization and placebo controls should be explained;

4) A description of any foreseeable risks or discomforts to the subject, an estimate of their likelihood, and a description of what steps will be taken to prevent or minimize them; as well as acknowledgment of potentially unforeseeable risks;

5) A description of any benefits to the subject or to others that may reasonably be expected from the research, and an estimate of their likelihood;

6) A disclosure of any appropriate alternative procedures or courses of treatment that might be advantageous to the subject;

7) A statement describing to what extent records will be kept confidential, including examples of who may have access to research records such as hospital personnel, the FDA, and drug sponsors;

8) For research involving more than minimal risk, an explanation and description of any compensation and any medical treatments that are available if subjects are injured through participation; where further information can be obtained, and whom to contact in the event of research-related injury;

9) An explanation of whom to contact for answers to questions about the research and the research

subject's rights (include the name and phone number of the Principal Investigator (PI) and the phone number of the Clinical Center's Patient Representative;

10) A statement that research is voluntary and that refusal to participate or a decision to withdraw at any time will involve no penalty or loss of benefits to which the subject is otherwise entitled;

11) A concluding statement indicating that the subject is making a decision whether or not to participate, and that his/her signature indicates that he/she has decided to participate having read and discussed the information presented.

When appropriate, or when required by the IRB, one or more of the following elements of information will also be included in the consent document:

1) If the subject is or may become pregnant, a statement that the particular treatment or procedure may involve risks, foreseeable or currently unforeseeable, to the subject, or to the embryo or fetus;

2) A description of circumstances in which the subject's participation may be terminated by the investigator without the subject's consent;

3) Any costs to the subject that may result from participation in the research;

4) The possible consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation;

5) A statement that the PI will notify subjects of any significant new findings developed during the course of the study that may affect them and influence their willingness to continue participation;

6) The approximate number of subjects involved in the study.

The consent process and document shall not include language waiving or appearing to waive any legal rights of the subject or releasing or appearing to release the investigators, sponsor, or institution from liability.

III. Approval of Informed Consent

Written consent documents must be approved by the IRB along with the written research protocols. Amendments or other changes in the approved protocol that affect informed consent must be incorporated into a revised consent document and approved by the IRB prior to use. Minor changes may sometimes be approved by expedited review. The consent document must be reviewed and approved by the IRB, at least once a year.

Consent documents and protocols involving the research use of ionizing radiation must also be reviewed by the Radiation Safety Committee and, if indicated, by the Radioactive Drug Research Committee. See Medical Administrative Series MAS 93-1, “Research Involving Human Subjects at the Clinical Center: Structure and Process."

In certain circumstances prescribed by the Federal regulations (45 CFR 46), an IRB may waive the requirement to obtain informed consent, or may approve a consent process which alters or does not include some of the elements above. For more information see NIH Multiple Project Assurance F.3.

The IRB also has the authority to have IRB members observe the consent process or to require that an impartial third party observe the consent process.

Copies of the approved consent form for a protocol will also be kept in the IRB files and the files of the CC Medical Record Department, Protocol Coordination Service Center.

IV. Responsibility for Obtaining Informed Consent

It is the responsibility of the Principal Investigator (PI) to ensure that informed consent is obtained. This includes ensuring that the subject is decisionally capacitated and that the potential risks and benefits of the research have been explained.

Written consent must be obtained by the PI, or by a PI-designated member of the research team who is knowledgeable about the protocol.

Although it is the responsibility of the PI to ensure that consent is obtained, it is the responsibility of all members of the research and health care team to ensure that the highest standards for informed consent are met.

Any member of the health care or research team who questions the decision-making capacity of the prospective subject or legally authorized representative, is obligated to make this known to the PI. For an adult subject unable to provide his or her own consent, procedures contained in policy MAS 87-4, "Consent Process in Research Involving Impaired Human Subjects," are to be followed.

The consent document must be signed and dated by (a) the subject or his/her legally authorized representative, (b) the PI or designee obtaining the consent, and (c) a witness to the signature. Each page of the consent document should be labeled with the subject's name and hospital number.

The subject is given a copy of the signed consent document. The original signed consent document is filed in the subject's permanent medical record under section IV, divider "Protocol Consent." In cases where subject accrual occurs outside the CC, signed consent documents are retained according to the policies of the institution where the patient received care.

V. Informed Consent for Non-Investigational Procedures

When non-investigational procedures are required for the care of a CC research subject, it is the responsibility of the individual performing the procedure to ensure that adequate informed consent is obtained.

Written consent must be obtained by the individual performing the procedure or by his/her designee who is knowledgeable about the procedure.

In special circumstances, for non-investigational procedures which are indicated for a subject who cannot provide his or her own consent, and for whom the legally authorized representative is not present, telephone consent from a legally authorized representative

may be obtained. When consent is obtained by telephone, the conversation should be monitored by a third party. A note explaining the circumstances and manner of obtaining consent and the name of the person providing consent should be entered in the medical record. For all other issues related to consent for persons who cannot provide their own consent, refer to MAS 87-4, "Consent Process in Research Involving Impaired Human Subjects," or MAS 92-5, "Research Involving Children and Children's Assent to Research."

VI. Use of Separate Consent Forms or Policies for Specific Procedures

Separate written informed consent, in addition to protocol consent, shall be obtained in certain circumstances, regardless of whether or not procedures are a direct part of the research protocol. Examples include:

1) NIH-549 Authorization for Public Information Audiovisual Materials Involving Patients
2) NIH-628 Authorization for Treatment, Tests, and Procedures on a Minor Patient
3) NIH-661 Doctor's Order and Patient Authorization for Clinical Photography
4) NIH-1225-1 General Admissions Consent and NIH-1225-2 Addendum to General Admission Consent for Minors
5) NIH-2514-4 Consent for Transfusion of Blood Components
6) NIH-2731 Informed Consent to Voluntary Sterilization. See also MAS 92-20, "Voluntary Sterilization of CC Patients"
7) NIH-2753 Information Practices
8) NIH-2626 Request for Administration of Anesthesia and for Performance of Operations and Other Procedures

For surgical procedures and other single invasive procedures, NIH-2626 should be completed within seven days prior to the procedure. Any procedure previously consented to but not initiated within 7 days of signing the consent form shall not be performed until a new consent is obtained. The time and date of the consent shall be recorded on the consent document.

For surgical inpatients, the NIH-2626 shall be completed prior to the administration of preoperative medication and prior to the patient's leaving the nursing unit. For surgical outpatients, consent must be obtained during the pre-surgery clinic visit. No patient shall be transported to the Operating Room before Form NIH-2626 has been properly executed.

The attending surgeon or physician who will perform the invasive procedure is responsible for the consent process for any procedures which require completion of NIH-2626. The responsible physician or designee shall explain in detail the nature, purpose, risks and benefits of the procedure. This explanation will be in language which the subject understands.

A detailed summary of the informed consent discussion must be documented in the patient's record or in the relevant sections of NIH-2626.

The Medical Staff Handbook should be consulted for a current list of procedures requiring the completion of NIH-2626.

9) MAS 89-1, “HIV Testing” and NIH-2663 Informed Consent Statement for HIV Blood Testing
10) MAS 93-11, “Administration of Blood Products to Jehovah's Witnesses”

VII. Oral Informed Consent and Non-English Consent

Under certain circumstances, the IRB may approve an oral consent process (see 45 CFR 46.117(b) (2)). In this case, the IRB must approve a written summary of what is to be said to the subject or legally authorized representative. A short written consent form stating that the elements listed in part II above (and required by 45 CFR 46.116) were presented orally to the subject should be signed by the subject and a witness who observed the presentation of information. The short summary should be signed by the person obtaining consent and the witness.

For the subject who is illiterate or blind, in addition to the requirements of 45 CFR 46.116 or 117 (as above), where possible, a

summary in a form that the subject can review (e.g., tape recording, braille document, video, etc.) should be provided to the subject or his/her representative.

For a protocol in which it is expected that the majority of subjects will not speak English, the consent document should be translated at least into the majority language of the subject population. If there is a prospective subject who does not speak or read English for a protocol in which the consent document has not been translated, the consent process will follow the process for oral consent and the information will be explained by someone who speaks the language of the subject.

VIII. Consent for Postmortem Examination

At the Clinical Center, post-mortem examination (autopsy) and disposal of a subject's body shall be permitted upon written or telegraphic consent of the responsible individual in accordance with the laws of the State of Maryland and the United States. The following forms should be utilized for these purposes:

SF-523 Authorization for Autopsy
NIH-1286 Relative's Instructions Regarding Disposition of Body
SF-523A Disposition of Body.

There may be protocols in which post-mortem examination is desired for scientific reasons. In such cases, protocol consent discussions should include consideration of autopsy. Where appropriate, consent documents should provide the subject an opportunity to indicate preferences about post-mortem examination (e.g., a check-off item). Consent for postmortem examination, however, will be obtained from the legally authorized representative or next of kin.

Consent for organ or tissue donation will be obtained from legally authorized representative or next of kin and the procedures outlined in policy MAS 90-1, “Organ and Tissue Donation,” should be followed.

IX. Obtaining Consent from Someone Not at the Clinical Center

For investigational procedures or research protocols that involve obtaining consent via technology and/or electronic process, rather than in person, review and approval must first be obtained from the Institute Clinical Director and the relevant IRB.

X. Consent for Emergency Procedures

In the case of an emergency, consent should be obtained from the subject. If the subject is unable to provide consent for non-investigational emergency procedures the legally authorized representative will provide consent. When consent is obtained by telephone, the conversation should be monitored by a third party. A note explaining the circumstances and manner of obtaining consent, and the name of the person providing consent should be entered in the medical record. The caregiver documenting the consent in the medical record shall sign and date the entry. In the event that no one is available or reachable to provide consent in a clinical emergency, treatment may be given in accordance with standard clinical practice.

Investigational emergency procedures must be part of a protocol previously approved by the relevant IRB.